AGGGAGAGTCTGCCCACAAGTTTTTGTATATTTTCTCACTGAGGCATCTATTCAGTTTGGGCAGCAGACA
CTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCAGCACTCAGAAGACGGAGGCA
GGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAGTCAGTTGGAAGTCAGCCAGCTTAGACAACA
TGGAGAGCCTGTGCCGAAAGCCACTGGGTAAGCCCGAATCTCAGTAGCAGAGAGCTGCCCAGGGTGCGTA
CTGC:AAAAAAAAAACCTCAAACAACAGAAGTAGGGAGGTGTAAAATAAAGTGTAGGGGGGTGGAATTTA
AGCTGATGTGGACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAAC
TGTCTATCAGAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGGGGCCTCTGGCT
TTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTATAAATTCACCATGAGCTTTAAC
ATCTTCTTTGTCATTTCGCAGACTGAGCCATGGAGTCTTTCGATGCTGACACCAATTCAACTGACCTACA
CTCACGGCCTCTGTTTCAACCCCAAGACATTGCCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGA
CTGCTAGGCAATGGGCTGGTGCTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGT
TCCTCCATCTCACCCTGGCCGATTTCCTCTGCTGCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATTCT
CCAAGGACACTGGCCCTATGGCTTGTTCCTGTGCAAACTTATCCCATCCATCATTATTCTCAACATGTTT
GCCAGTGTCTTCCTGCTTACTGCCATTAGCCTGGACCGATGTCTGATAGTACATAAGCCAATCTGGTGCC
AGAATCATCGAAACGTGAGAACCGCCTTCGCCATCTGTGGATGTGTCTGGGTGGTAGCCTTTGTGATGTG
TGTGCCCGTATTTGTATACCGTGATCTGTTCATTATGGACAATCGCAGTATATGTAGATATAATTTTGAT
TCCTCCAGGTCATATGATTATTGGGACTACGTGTACAAACTAAGTCTACCAGAAAGCAATTCTACTGATA
ACTCCACTGCTCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCCTCTGTACAGGCAAGGGATTA
CTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCCTAACATCTCCTGAAGACTCATTCTCTCTA
GATTCAGCAAACCAACAACCCCATTATGGTGGAAAGCCTCCTAATGTCCTCACAGCCGCCGTACCCAGCG
GGTTTCCTGTTGAAGATCGTAAATCCAATACACTGAACGCTGACGCTTTTCTCTCTGCTCACACAGAACT
TTTCCCTACTGCTTCTAGTGGTCATTTATACCCCTATGATTTCCAGGGGGATTATGTTGACCAATTCACG
TATGACAATCATGTGCCGACACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCCTGGTGC
CGTTTTTCATCATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCAACTTCACCAAGTC
TCGGAACAAAACCTTTCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTTTATCTGCTGGACTCCATACCAT
CTTGTCGGAGTCCTGCTATTGATTACTGATCCAGAAAGTTCCTTGGGGGAAGCTGTGATGTCCTGGGACC
ACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCTTCAACCCCTTTCCTGTATGCCCTCTTGGGGAAAGA
CTTTAGGAAGAAAGCAAGACAGTCTATAAAGGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCAC
TCTACCAACTGTACCCAAGACAAAGCCTCTTCAAAAAGAAACAATATGAGTACAGATGTGTGAAGATGTG
GCCCTGGGAACCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTAGACA
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TTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCCATGGGACCAGTGTTTAACAGGCCTTC
TTGTTTCCATCAGTGTTAAGTTTTACCTCATTTGGCTTAGTCTATTCCCATCCCTGACTACACCATGTGC
AATGAATAACTTTTTCATCTGTTTTCAGTATTCTTTTTTTTTCCTTAGCATCATCTAAACTTCTAGTTTG
CATGGAAGGCTGCTCTTATTGTTCTGAATGGAAGATATTCATTTATTGTACAGTTTTGTGGTGGTGACAA
GTGATTTTTAAGTGGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTTGAGTTAGAGT
TTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAGTGTTCATGTGAGCA
AGTGAGCACAGATACACATAAACACTTTCCTACTCCTGGAGTGTTTTAGAAGTTGTAGCTTGGAGCTC
(SEQ ID NO:1)

MESFDADTNSTDLHSRPLFQPQDIASMVILGLTCLLGLLGNGLVLWVAGVKMKTTVNTVWFLHLTLADFLCC
LSLPFSLAHLILQGHWPYGLFLCKLIPSIIILNMFASVFLLTAISLDRCLIVHKPIWCQNHRNVRTAFAICGCVWV
VAFVMCVPVFVYRDLFIMDNRSICRYNFDSSRSYDYWDYVYKLSLPESNSTDNSTAQLTGHMNDRSAPSSV
QARDYFWTVTTALQSQPFLTSPEDSFSLDSANQQPHYGGKPPNVLTAAVPSGFPVEDRKSNTLNADAFLSA
HTELFPTASSGHLYPYDFQGDYVDQFTYDNHVPTPLMAITITRLVVGFLVPFFIMVICYSLIVFRMRKTNFTKS
RNKTFRVAVAVVTVFFICWTPYHLVGVLLLITDPESSLGEAVMSWDHMSIALASANSCFNPFLYALLGKDFRK
KARQSIKGILEAAFSEELTHSTNCTQDKASSKRNNMSTDV (SEQ ID NO:2)

**FIGURE 1**

underlined = deleted in the targeting construct (SEQ ID NO:5)

[ ] = sequence flanking Neo insert in targeting construct (SEQ ID NO:6 and SEQ ID NO:7)

```
AGGGAGAGTCTGCCCACAAGTTTTTGTATATTTTCTCACTGAGGCATCTATTCAGTTTGG
GCAGCAGACACTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCA
GCACTCAGAAGACGGAGGCAGGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAG
TCAGTTGGAAGTCAGCCAGCTTAGACAACATGGAGAGCCTGT [GCCGAAAGCCACTGGGT
AAGCCCGAATCTCAGTAGCAGAGAGCTGCCCAGGGTGCGTACTGCAAAAAAAAAACCTC
AAACAACAGAAGTAGGGAGGTGTAAAATAAAGTGTAGGGGGGTGGAATTTAAGCTGATGT
GGACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAA
CTGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGG
GGCCTCTGGCTTTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTAT
AAATTCACCATGAGCTTTAACATCTTCTTTGTCATTTCGCAGACTGAGCCATGGAGTCTT
TCGATGCTGACACCAATTCAACTGACCTACACTCACGGCCTCTGTTTCAACCCCAAGACA
TTG] CCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGACTGCTAGGCAATGGGCTG
GTGCTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGTTCCTCCAT
CTCACCCTGGCCGATTTCCTCTGCTGCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATT
CTCCAAGGACACTGGCCCTAT [GGCTTGTTCCTGTGCAAACTTATCCCATCCATCATTAT
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AGTACATAAGCCAATCTGGTGCCAGAATCATCGAAACGTGAGAACCGCCTTCGCCATCTG
TGGATGTGTCTGGGTGGTAGCCTTTGTGATGTGTGTGCCCGTATTTGTATACCGTGATCT
GTTCATTATGGACAATCGCAGTATATGTAGATATAATTTTGATTCCTCCAGGTCATATGA
TTATTGGGACTACGTGT] ACAAACTAAGTCTACCAGAAAGCAATTCTACTGATAACTCCA
CTGCTCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCCTCTGTACAGGCAAGGG
ATTACTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCCTAACATCTCCTGAAG
ACTCATTCTCTCTAGATTCAGCAAACCAACAACCCCATTATGGTGGAAAGCCTCCTAATG
TCCTCACAGCCGCCGTACCCAGCGGGTTTCCTGTTGAAGATCGTAAATCCAATACACTGA
ACGCTGACGCTTTTCTCTCTGCTCACACAGAACTTTTCCCTACTGCTTCTAGTGGTCATT
TATACCCCTATGATTTCCAGGGGGATTATGTTGACCAATTCACGTATGACAATCATGTGC
CGACACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCCTGGTGCCGTTTT
TCATCATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCAACTTCACCA
AGTCTCGGAACAAAACCTTTCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTTTATCTGCT
GGACTCCATACCATCTTGTCGGAGTCCTGCTATTGATTACTGATCCAGAAAGTTCCTTGG
GGGAAGCTGTGATGTCCTGGGACCACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCT
TCAACCCTTTCCTGTATGCCCTCTTGGGGAAAGACTTTAGGAAGAAAGCAAGACAGTCTA
TAAAGGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCACTCTACCAACTGTACCC
AAGACAAAGCCTCTTCAAAAAGAAACAATATGAGTACAGATGTGTGAAGATGTGGCCCTG
GGAACCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTA
GACAATTTGGCGACTCTCAGAGAAAGGTCTCTTATTGACATCAGCATCATTTGAAAACAT
TAAAGATGCAAAATTTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCCATG
GGACCAGTGTTTTAACAGGCCTTCTTGTTTCCATCAGTGTTAAGTTTTACCTCATTTGGC
TTAGTCTATTCCCATCCCTGACTACACCATGTGCAATGAATAACTTTTTCATCTGTTTTC
AGTATTCTTTTTTTTTCCTTAGCATCATCTAAACTTCTAGTTTGCATGGAAGGCTGCTCT
TATTGTTCTGAATGGAAGATATTCATTTATTGTACAGTTTTGTGGTGGTGACAAGTGATT
TTTAAGTGGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTTGAGTTA
GAGTTTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAG
TGTTCATGTGAGCAAGTGAGCACAGATACACATAAACACTTTCCTACTCCTGGAGTGTTT
TAGAAGTTGTAGCTTGGAGCTC
```

**FIGURE 2A**

**Gene Sequence Structure \***

663 bp          Sequence Deleted          859 bp

**Size of full-length cDNA:** 2658 bp

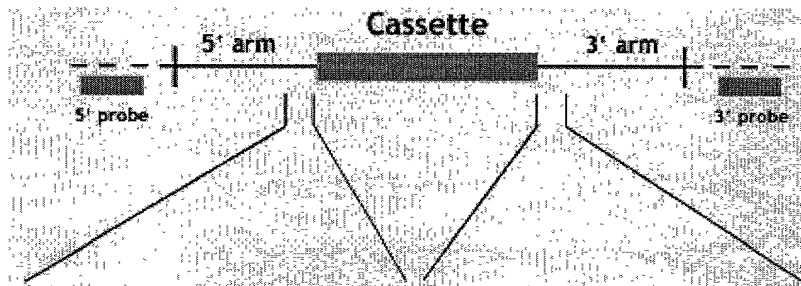**Targeting Vector\* (genomic sequence)**

Construct Number: 3036

LacZ-Neo

Cassette

5' arm          3' arm

5' probe          3' probe

Arm Length:
5': 3.2 kb
3': 1.8 kb

——— Targeting Vector
- - - - - Endogenous Locus

\* Not drawn to scale

```
5'>CGAGGTTCTGTGAGGGGGGCC
TCTGGCTTTGAGAGGGTGTACCAT
CACATAAGACTCCTAAAAGCACAT
ACTTTTATAAATTCACCATGAGCT
TTAACATCTTCTTTGTCATTTCGC
AGACTGAGCCATGGAGTCTTTCGA
TGCTGACACCAATTCAACTGACCT
ACACTCACGGCCTCTGTTTCAACC
CCAAGACATTG<3'
(SEQ ID NO:3)
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5'>GGCTTGTTCCTGTGCAAACTT
ATCCCATCCATCATTATTCTCAAC
ATGTTTGCCAGTGTCTTCCTGCTT
ACTGCCATTAGCCTGGACCGATGT
CTGATAGTACATAAGCCAATCTGG
TGCCAGAATCATCGAAACGTGAGA
ACCGCCTTCGCCATCTGTGGATGT
GTCTGGGTGGTAGCCTTTGTGATG
TGTGTGCCCGT<3'
(SEQ ID NO:4)
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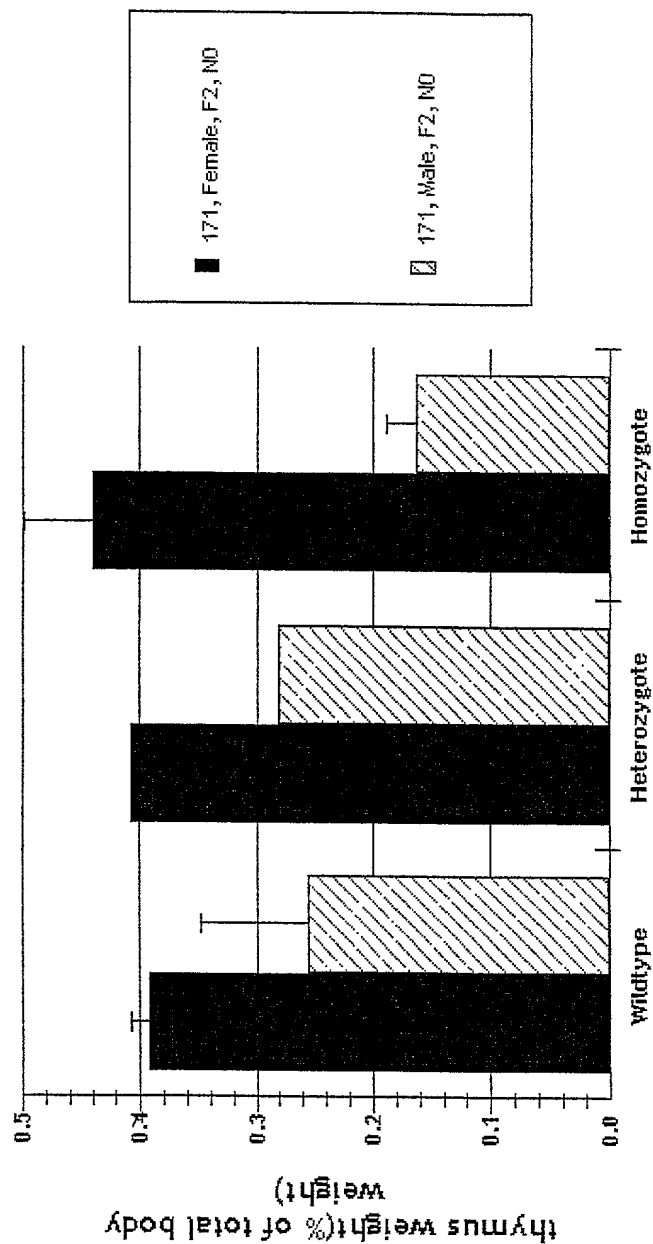# FIGURE 2B

necropsy - thymus weight/body weight



| 171, Female, F2, N0 |
| 171, Male, F2, N0 |

thymus weight(% of total body weight)

Wildtype  Heterozygote  Homozygote

**FIGURE 3**

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